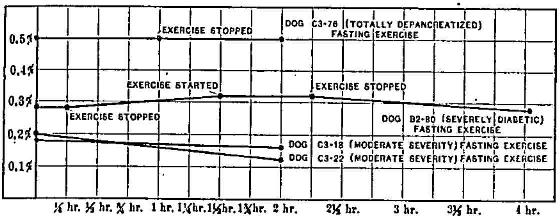

Chart V.—Exercise in severely diabetic dogs.

RETENTION OF PROTEIN DURING DIET REDUCTION TO RELIEVE THE GLYCOSURIA IN DIABETES MELLITUS.

By R. L. Fenlon, M.D.,

IOWA CITY, IOWA.

(From the Laboratory of Chemical Research of the Department of Internal Medicine, State University of Iowa.)

There was recently reported from this clinic a dietetic treatment of diabetes mellitus.[1]

The procedure is essentially the maintenance of the protein intake at a moderate level, the restriction of the fat and the relatively rapid reduction of the carbohydrate until the patient's glycosuria disappears. The carbohydrate tolerance is then built up by a gradual increase in the carbohydrate intake (starvation days are dispensed with). The treatment is controlled by daily twenty-four-hour urine analyses and frequent blood analyses.

Some 15 cases were reported in the earlier paper. At the present writing 40 cases (63 admissions) have been treated under this method of protein retention in the diet.

The mortality was 5 per cent. (2 cases). One of these two was a case of carcinoma of the prostate gland, with retention of urine and a mass in the left lower abdomen; the patient died the second day postoperative. The other case was a refractory patient who had been in the hospital for three admissions. At no time would he follow the prescribed diet, and died of diphtheria and a lung abscess; pure culture of Klebs-Loeffler bacilli were obtained from the bronchi and abscess cavity at necropsy.

With the exception of one case, which showed a slight amount of acetone, all cases were sugar- and ketone-free upon discharge.

There is a gradual reduction in acetone and diacetic acid from the beginning of dietary treatment.

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[1] Fenlon, R .L.: Diet Reduction with Retention of Protein to Relieve Glycosuria in Diabetes Mellitus, Bost. Med. and Surg. Jour., February 12, 1920, No. 7, clxxxii, 168–171.

All but one of the cases coming under observation a second time have increased in weight.

This method of relieving glycosuria in diabetes mellitus and of subsequently establishing the dietary tolerance has been found applicable to patients of all ages.

General Outline of Treatment. Examination of the patient.

(*a*) When a case is admitted a careful history is taken by the medical intern in charge, special note being made as to the age of the patient, the duration of the symptoms and the severity of the disease, the complications, if any are present and the diet followed before entrance to the hospital.

(*b*) A complete physical examination.

(*c*) Routine blood and urine analyses are made, *i. e.*, blood sugar and fat; urine sugar acetone and diacetic acid.[2]

According to the data collected in the above-mentioned examination the treatment to be followed in the particular case is determined, and each case is classified a severe, moderate or mild type to facilitate its subsequent treatment.

The severe type includes all patients under twenty-one years of age, even though the diabetes may appear mild; all cases showing the three cardinal urinary findings acetone, diacetic acid and sugar; cases having a hyperglycemia accompanied by a hyperlipemia and those showing a tendency toward coma. Into the group of moderate diabetics fall all those showing sugar and acetone in the urine or having hyperglycemia, with slight or no hyperlipemia.

The mild type includes cases showing only sugar in the urine and having a hyperglycemia, with only slight or no hyperlipemia.

Method of Establishing a Carbohydrate Tolerance. While under treatment (after the glycosuria has been overcome) the amount of carbohydrate is raised each day, particular care being exercised to avoid the reappearance of sugar in the urine. In this series a "break" (glycosuria) occurred in 7.5 per cent. of the cases. The reason for avoiding a "break" is that a patient going out of the hospital without glycosuria appearing when the arbitrary carbohydrate tolerance is reached has a more stable outlook than one who is discharged with a weakened sugar function as shown by the recent "break."

It is evident that the most of these cases have been sent out on what might be termed an arbitrary carbohydrate tolerance; in other words, on a daily intake which is lower than the actual tolerance, a margin of safety is thus provided. The factors entering into the determination of this are the specific gravity of the urine, the severity of the case, the amount of urine passed in twenty-four hours and the hunger as expressed by the individual.

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[2] Blood fat by Bloor's method. Blood sugar by Benedict Myers's method. Acetone by Rothera's Reaction. Diacetic acid by Gerhardt's method.

The specific gravity reading varies in each case at the time the patient is sugar-free. As the dietary treatment progresses the specific gravity generally decreases somewhat below this point. As the carbohydrate intake increases toward the arbitrary tolerance the specific gravity gradually approaches the level of the first sugar-free reading. In most cases it is not advisable to further increase the carbohydrate intake after the specific gravity reading rises to this level.

The severity of the disease as shown by the urinary and blood findings at the onset of the treatment and deductions drawn from the individual case give an approximate knowledge of the patient's tolerance.

The daily amount of urine passed also is an indication to a slight extent. As an example, when the succeeding daily amounts fluctuate markedly in the following manner, 1200 c.c., 2100 c.c., 1150 c.c., 1900 c.c. it is well to be cautious with the carbohydrate increase.

The final and most important point is the hunger of the patient. It is not advisable to raise the diet in carbohydrate when the patient maintains that his food intake is sufficient. No definite caloric intake (according to the weight of the individual) is followed in the treatment at this hospital. The final diet is adjusted to suit the wants of the patient. In a very few cases the diet was increased after the hunger was satisfied and glycosuria resulted.

Fehling's test for sugar in the urine as used here follows: Equal amounts of "A" and "B" solutions are mixed in a test-tube (2 or 3 c.c. of each) and boiled in a water-bath. One c.c. of urine is added and the boiling continued. There may be no direct reduction when hot, but the reduction may appear when the tube and contents are set aside to cool.

Dietary Treatment Used to Relieve Glycosuria in Severe Cases. In cases six or seven years old 35 to 40 grams of protein per day are given, the amount being increased with the age and size of the patient. An adult receives 70 to 80 grams per day. This protein level is maintained throughout the patient's stay at the hospital unless a higher caloric diet is desired upon discharge; at that time the protein allowance may be increased.

Fat is eliminated from the diet on the day of admission and is the last constituent to be replaced.

The daily carbohydrate intake in these cases is placed at from 130 to 140 grams and is maintained at this level for two or three days.

Accessory treatment at the onset consists in bed-rest, retention of body heat with blankets, forced warm drinks (fat-free broths, weak tea or coffee and warm water). The rate of forcing these fluids depends upon the amount of urine eliminated in twenty-four hours, the object being to keep the fluid intake at a level slightly greater than or equal to the fluid output.

To summarize: The protein is kept at a constant relatively high level (35 to 40 grams in children, 70 to 80 grams in adults), the fat is practically eliminated and the carbohydrate is at 130 to 140 grams. The next step in the diet reduction is the diminution of the carbohydrate 10 or 15 grams a day until the patient's glycosuria is relieved. If the glycosuria does not disappear when but 10 grams of carbohydrate per day are given the treatment as outlined in a previous paper is followed.[3]

"Third Step. If glycosuria is still present add 50 to 100 grams of oatmeal to the diet for two days.

"Fourth Step. If glycosuria persists, repeat the diet used just preceding the oatmeal days, lowering the proteins one-third. Keep the patient two days on this diet if necessary.

"Fifth Step. If not aglycosuric, starve, giving only fat-free broths and water for a two-day period.

"Sixth Step. If necessary revert to the oatmeal diet for two days and again starve."

During the period of low caloric intake the calories may be increased by the use of alcohol. Alcohol (as whisky) has not interfered in any way with the establishment of a sugar tolerance in this series of cases.

When the patient becomes aglycosuric (at which time he is generally diacetic acid-free and showing less acetone in the urine) the carbohydrate is increased 1 gram per day in the young or 3 grams per day in adults. The fat is gradually increased when the carbohydrate totals 18 to 20 grams, but is kept at least 10 grams lower than the carbohydrate until the laboratory tests indicate that the carbohydrate tolerance has been reached. The fat at that time may be gradually raised to the same level as the protein or even 5 grams higher. The allowance of fat in the final diet is checked by a blood fat. The patient is then instructed to return to his home for a period of two or three months since this diet, as a rule, provides sufficient calories for the time being and will give a rest to the metabolic mechanism.

At the end of this time a return to the hospital is advised when a readjustment of the diet is made, the amount of carbohydrate being increased and the fat or protein changed if necessary.

The long period of diet reduction in this type of diabetes is invaluable for overcoming the hyperlipemia. One case treated as outlined above came in with a blood fat of 1.14 per cent. and was discharged with a blood fat of 0.596 per cent. A second case upon admission showed 2.28 per cent. blood fat; three weeks later 1.14 per cent., a reduction of $\frac{11}{15}$ of the hyperlipemia was noted, and upon discharge the blood fat had been reduced to 0.91 per cent. Other cases with less marked hyperlipemia had a normal blood fat upon discharge. These cases all had negative urines upon discharge, *i. e.*, neither sugar, acetone nor diacetic acid was present.

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[3] Loc. cit.

Case History and Chart of Mr. F. L. Clinical Number, 7230.

Complaints. Excessive urination and weakness of the calves and wrists.

Social History. White male, aged fifty years; farmer. No venereal history.

Family History. Negative.

Past Medical History. Digestive system: Has always had a very good appetite. His wife often said that he ate too much. Always drank lots of water. Occasionally some belching and heartburn. Otherwise negative.

Present Illness. Began about May, 1919, with nocturnal frequency and excessive twenty-four-hour urine. The urine looked like salt water. Had to void five or six times at night. He could eat like a trooper. Had difficulty in satisfying his thirst, went to a physician and was diagnosed diabetes. Later went to another physician who made the same diagnosis and placed the patient on a diet of eggs, fish, meats and fats, but no sweets. Advised the patient to eat fats and to drink cream. Could not follow this diet longer than six months. Began to be a little deaf nine months ago and has had trouble with vision. At present complains of weakness in the calves of the legs and wrists and excessive urination. Best weight, 180 pounds. Present weight, 147 pounds.

Day.	Sugar.		Acetone.	Diacetic acid.	Protein	Fat.	Carbohydrate.
	Per cent.	Gm.					
1	6.0	178	++++	+++	82	8	123
2	5.1	132	+++	++	84	7	141
3	6.0	175	+++	++	80	5	133
4	5.4	142	+++	++	88	19	110
5	5.7	166	++	++	90	15	100
6	5.4	122	++	++	85	12	88
7	5.4	143	++	+	85	8	81
8	5.1	109	++	+	85	8	70
9	3.3	101	++	+	85	10	58
10	2.0	73	++	tr.	85	13	50
11	1.9	77	++	tr.	82	19	40
12	1.3	57	++	s. tr.	85	8	31
13	1.0	44	+	v. s. tr.	85	8	27
14	0.7	22	tr.	v. s. tr.	80	7	21
15*	0.2	6	s. tr.	v. s. tr.	84	7	16
16	0.5	28	s tr.	v. s. tr.	86	6	14
17	0.4	24	s. tr.	v. s. tr.	80	6	15
18	0.2	11	s tr.	v. s. tr.	83	10	9
19	0	0	v. s. tr.	0	81	6	8
20	0	0	v. s. tr.	0	80	7	10
21	0	0	v. s. tr.	0	83	9	12
22	0	0	0	0	83	8	15

* 4 P.M. urine specimen was sugar-free. Sugar (by mistake) was served with evening meal.

Tr. = trace. S. tr. = slight trace. V. s. tr. = very slight trace.

Blood on first day = sugar, 0.454 per cent.; fat, 2.28 per cent.

Physical Examination. Mucosa of mouth and throat is red and dry. Tongue is dry and fissured. Acetone odor to breath. Skin dry and desquamating. Muscles everywhere atrophied and show myoidema. Otherwise negative.

Laboratory Findings. Serum Wassermann negative.

Urine examination: Specific gravity, 1038. Sugar, 6 per cent. Acetone, ++++.

Diacetic, +++ (blue-black).

Blood: Sugar, 0.454 per cent.; fat, 2.28 per cent.

Blood count normal.

Patient was seen again six weeks after discharge, active in farm work and had gained 12 pounds in weight.

The Treatment Followed in the Moderate Type of Diabetes. 80 to 90 grams of protein are given. This amount is not changed except just before discharge, when it may be increased if so desired; 12 to 15 grams of fat daily are allowed in order that the diet may be more palatable. The same amount of carbohydrate as protein is included in the diet. As an example the diet at the beginning of the treatment will be 90 grams protein, 15 grams fat and 90 grams of carbohydrate.

The carbohydrate is then reduced 15 to 20 grams daily until the urine is sugar-free. The carbohydrate is then increased 5 to 8 grams daily until the tolerance is reached. When the diet contains 50 grams or more of carbohydrate the fat is increased 10 to 15 grams per day until the total amount is not more than 10 grams above the next highest constituent (either protein or carbohydrate).

The treatment is varied as follows in cases with nephritis: In adult cases with nephritis the protein is kept at 60 grams daily. The reduction of the carbohydrate from 90 to 100 grams is made slowly, *i. e.*, 10 grams daily; until the patient is aglycosuric. Fat and carbohydrate are increased as above.

Two cases of diabetes and nephritis associated with gangrene have been treated in this series, and in both instances the gangrene cleared up before the patient's discharge from the hospital.

Treatment Followed in Mild Type. Protein and the carbohydrate are placed at 100 grams daily; fat at 20 to 30 grams.

The carbohydrate is halved daily until the urine is sugar-free and is then increased 10 grams per day until the tolerance is reached. When the carbohydrate reaches 60 grams the fat is added 25 to 30 grams daily until the total amount is not over 15 grams higher than the next highest constituent of the diet.

Case History of Mr. O. L. Clinical number, 6999.

Entrance Complaint. Poor vision and inability to hold his urine.

Social History. White male, aged sixty-two years farmer. No venereal history.

Family History. Negative.

Past Medical History. Malaria at age of twelve years. Typhoid at thirty-six. Thirty-two boils on the back of his neck and in his hair three years ago. Swelling of the ankles during the day for the past two years. Good deal of cramping of the muscles of the legs and thighs the past seven or eight years. Appetite always very good. For the past twelve years has had spells of excessive thirst, and has never missed getting up from two to six times to urinate at night. Often wets his clothes. Poor sleeper the past five or six years. Has been seeing double lately. Has staggered a little, assigned to weakness of the legs.

Present Illness. Inability to hold urine began about twelve years ago and was gradual in its development. Worse at times, especially when he would get thirsty and drink a lot of water. Would have to get up at night to urinate and passed one to two gallons of urine in twenty-four hours. Appetite always good, but has had a special craving for sweets. Often noticed that bees would gather and apparently feed on his urine. For the first three years he used bran bread, and this seemed to help a good deal. Sugar was found in the urine and the patient told that he had diabetes. Has eaten nothing that he knew contained starch or sweets for the past twelve years, excepting pies; he, however, uses sugar in tea and coffee. Always had a preference for fat meat. Noticed that he was getting weaker about two years ago. Skin is dry but never itched. In July, 1919, the patient's vision began to fail. Saw double. Seemed to have a smoky scum over the left eye and could only see with this eye when he looked sideways. Weighed 270 pounds when thirty years old. Maintained about the same weight until he was forty. Lost weight up to fifty (onset of present illness). Present weight, 212 pounds.

Physical Examination. Arcus senilis marked in both eyes. Pupils react to light and accommodation. Left pupil slightly oval in shape. Definite Romberg test. Misses heel to knee test. Walks with a wide base. Ataxic. Knee-kicks and tendo achillis only present on reinforcement. Bilateral neuritis of the nervus cochlearis. Diabetic retinitis.

CHART OF TREATMENT OF MR. O. L.

Day.	Sugar.		Acetone.	Diacetic acid.	Blood.		Protein.	Fat.	Carbohydrate.	Calories.
	Per cent.	Gram.			Sugar.	Fat.				
1	2.2	20	0	0	0.263	0.857	94	6	105	850
2	1.1	13	0	0	....	....	94	8	90	808
3	0.0	0	0	0	....	....	90	16	47	692
4	0.0	0	0	0	....	....	94	12	36	628
5	0.0	0	0	0	....	....	93	23	62	827
6	0.0	0	0	0	....	....	97	31	75	967
7	0.0	0	0	0	....	....	98	43	84	1155
8	0.0	0	0	0	....	....	98	66	80	1306
9	0.0	0	0	0	....	....	96	88	90	1536
10	0.0	0	0	0	....	....	98	108	100	1764
11	0.0	0	0	0	0.133	0.732	100	110	100	1790

Laboratory Findings. Blood count was negative except for an eosinophilia of 3 per cent. Serum Wassermann negative on two tests.

Weekly Fast Days. Weekly fast days do not enter into the treatment used either at the University Hospital or that subsequently followed by the patients in their homes.

The purpose of this treatment is to produce as stable a carbohydrate metabolism as possible. This is done by establishing the tolerance with small increments, 1 to 2 grams per day in all severe cases. In our opinion weekly fast days may defeat this purpose, in that the withdrawal of the carbohydrate and the rapid resumption of the load may tend to strain the sugar mechanism. Out of 38 cases so treated 8 have returned for an increase of the carbohydrate in the diet. None of these 8 cases have shown glycosuria while at home for periods of three to five months and the tolerance of all upon return has been set at a higher level.

Cases are advised to return to the hospital should they desire an increase in their diet; however, they are asked not to return in less than two months unless something untoward develops.

CHART OF RETURN CASES

Case.	Diet first discharge.				Diet second discharge.				Diet third discharge.			
	Pro.	Fat.	Cho.	Cal.	Pro.	Fat.	Cho.	Cal.	Pro.	Fat.	Cho.	Cal.
1	60	90	50	1250	85	85	75	1405	85	85	85	1445
2	65	75	45	1115	60	75	75	1215				
3	90	90	40	1330	100	100	80	1620				
4	40	35	31	600	70	70	50	1110				
5	70	90*	60	1330	100	115	85	1775				
6	100	100	85	1640	110	120	105	1940				
7	100	110	100	1790	100	100	115	1760				

* Discharged under previous method of treatment.

Case 1. Nineteen years old, slightly under weight. During first admission she "broke" on 40 gm. of carbohydrate.

Case 2. Slight build, no complaint of hunger.

Case 3. Tall, slender, "broke" on 46 gm. of carbohydrate (first admission).

Case 4. Boy, aged six years. Has gained in weight and plays with other children.

Case 5. Travelling man, aged thirty-three years.

Case 6. Male, aged twenty years. Plays basket ball on a town team, trapped and hunted between his two admissions and gained ten pounds in weight.

Case 7. See case report No. 6990.

Results from High Fat Diets. Some cases before entrance to the hospital had lived upon a diet rich in fats. The difficulties encountered while treating such cases suggested the following conclusions:

1. A longer period of time with a continuous low calorie diet was necessary to overcome the glycosuria and ketonuria.

2. Although the tendency of a high fat diet (especially with a low carbohydrate intake) to produce acidosis is well known; too little attention is paid to this point by the general practitioner. Many patients are advised by their physician to limit their sugar, bread, potato and starch intake, but no mention is made of the fat intake; in fact a few cases (see case report of Mr. F. L.) have been told to increase their fat consumption by eating cheese, butter, nuts, etc., and drinking cream.

3. High fat diets appear to cause a decrease in the carbohydrate tolerance; that is, with long-continued, high fat ingestion the carbohydrate seemingly cannot be placed at as high a level as the case should tolerate.

Foci of Infection. Demonstrable foci of infection such as diseased teeth, tonsils, etc. are removed during the patient's stay in the hospital, the diet being established before operation. The daily food intake (that is only the fat and carbohydrate) is reduced on the day of the operation and replaced slowly as the urinary picture clears.

Oatmeal Treatment. Oatmeal, because of its slow absorption and high potassium content, has been used recently in a few instances as the principal carbohydrate of the food intake during the diet reduction. Two-thirds of the daily carbohydrate is given as oatmeal. Results in a case follow: The first urine specimen received from this patient contained 12.5 per cent. of sugar. The urine was sugar-free after four days of diet reduction. Treatment was completed in sixteen days and then his tolerance was set at 100 grams of protein, 100 grams of fat and 75 grams of carbohydrate.

Case History of Mr. M. G. Clinical Number 7598.

Entrance Complaint. Diabetes.

Social History. White male, aged twenty years; single; farmer. No venereal history.

Family History. Negative.

Past Medical History. Light attack of influenza in the fall of 1918.

Present Illness. Began about five weeks ago with polyuria, which gradually increased until in two weeks he was passing thirteen pints of urine in twenty-four hours. He developed a ravenous appetite and drank large quantities of water. Two weeks before admission he consulted a physician, who found sugar in his urine. The diet recommended was to omit sugars and syrups and to reduce bread and potatoes to half the usual amount. After this the total twenty-four-hour urine decreased to an average of seven to nine pints. Weight two months ago was 158 pounds and at present 138 pounds. He has felt drowsy in the daytime during the past two weeks.

Physical Examination. Patient is a slender, fairly well-nourished, white male of twenty. Face is flushed. Skin on the body is dry. Tongue is semi-moist. Otherwise negative.

Laboratory Findings. Serum Wassermann negative on two tests. Blood count was negative except for an sosinophilia of 5 per cent. Urine: Specific gravity, 1052. Sugar, 12.5 per cent. Acetone and diacetic negative. Blood sugar, 0.270 per cent.

Some Dietary Regulations Which Are Deemed Advisable to Incorporate in the Treatment. 1. Milk and orange are to be excluded from the diet in severe cases. Milk because of its prompt assimilation is given only when the carbohydrate tolerance is above 30 grams; exception to this is made in cases of children. Orange tends to cause a glycosuria before the normal tolerance of the particular case is reached. In a few instances the feeding of orange caused a glycosuria which upon withdrawal of orange from the food was relieved and the carbohydrate was increased to a higher level without the reappearance of sugar in the urine. Grapefruit and rhubarb are used in the place of orange without the danger of causing glycosuria prematurely.

2. No cane sugar is to be given as such, regardless of the tolerance. Saccharin is to be used for sweetening.

3. The food is to be divided equally among the three meals of the day, *i. e.*, one-third of the protein, one-third of the fat and one-third of the carbohydrate are to be included in the breakfast, in the dinner and in the supper.

4. Bananas are not to be included in the diet when the tolerance, is less than 90 grams of carbohydrate.

Instructions Given to the Patient for His Use after Leaving the Hospital. While the patient is in the hospital he receives a course of instructions on his diet in which he becomes familiar with the food constitutents, protein, fat and carbohydrate, both as to the physiologic action, source and calorific value.[4]

After the patient has become familiar with the food value of most of the common food materials, he is taught to calculate a day's diet. Great stress is put upon the equal division of the food among the three meals of the day, *i. e.*, one-third of the protein, one-third of the fat and one-third of the carbohydrate at each meal.

Six days' diet are given to the patient when he leaves, and he is instructed to live only on a weighed diet. Since one-third of his food allowance for the day is given in each meal there can be a variety of the day's diets; for a breakfast of one day and a dinner of another and a supper of a third day can be taken with no danger of exceeding his tolerance. The patient is taught to substitute one food for another, so that he may vary his diet as the foods in season vary, and he is more content to live on a prescribed diet too when he can make slight changes to suit his individual taste. In order that no difficulty may arise in regard to the use of a balance for weighing the food, he is taught to weigh out foods on the balance that he is to use after leaving the hospital. This instruction enables the patient to calculate his own diet if he so desires.

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[4] Government Bulletin No. 28, Chemical Composition of American Food Products has been found helpful.

The doctor in charge gives the patient instructions in the qualitative urine tests for sugar and diacetic acid, and the patient is instructed to test the urine for sugar each day. He is told to use but 1 c.c. of urine in performing Fehling's test and is shown the various phases of reductions with this test when sugar is present, green, yellow and red. Instruction is given to reduce the carbohydrate of the diet slightly when a green or yellow reaction results and when the urine is again sugar-free to gradually return to the former level. He is instructed to return to the hospital if the reduction is persistently red. In case of an infection such as a severe cold, tonsillitis or other condition with increased temperature, the patient is advised to test his urine for the presence of diacetic acid with the ferric chloride solution, and if he finds the test to be positive to reduce the fat in his diet until the diacetic disappears, when he may gradually increase the fat until the former amount is being taken.

THE BACTERIOLOGY OF THE FASTING STOMACH AND DUODENUM: AN EXPERIMENTAL STUDY BASED ON THE FINDINGS IN THIRTY DOGS.

By Peter H. Poppens, M.D.,
CHICAGO, ILL.

(From the Pathological Laboratory of the Surgical Department of Rush Medical College.)

Clinically it has long been recognized that the upper portion of the gastro-intestinal canal contains relatively few pathogenic bacteria. Cushing and Livingood[1] found difficulty in recovering microörganisms from the mucous membrane of the stomach, duodenum and even the jejunum as far down as complete emptying of the canal occurred. Kohlbrügge[2] in discussing the autosterilization of the intestinal canal stated that the small bowel either has no bacteria at all or, when it does show them, that they belong to the colon group. On the other hand, as long ago as 1886, Escherich[3] showed that in infants B. coli predominates in the lower portion of the intestinal canal while Bacillus lactis aërogenes is found higher up. Gilbert and Dominici[4] examined the intestinal contents of dogs which were killed three hours after a meal of bread and meat. They found many organisms in the stomach, few in the duodenum and a gradually increasing number down the small bowel. Kendall[5] Hess,[6] Sisson,[7] Torrey[8] and others have obtained similar results.